

Original article

Study on the histopathology of chronic arsenicosis

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Abstract *Background* Arsenicosis is epidemic in Bangladesh. The associated cutaneous changes have high malignant potential.

Objectives To assess the spectrum of histopathological changes in arsenical keratoses.

Patients and methods A total of 70 arsenicosis patients (arsenic exposure group) and 20 clinically healthy patients (control group) who showed typical features of cutaneous manifestations were selected in this study. Skin biopsies from randomly selected patients were taken for undertaking histopathological studies.

Results In the arsenicosis group and control group different istoloicl cnes were hypekeratois (100% vs. 20%) [$p<0.001$], parakeratosis (97% vs. 10%) [$p<0.001$], acanthosis (95.7% vs. 1%) [$p<0.001$], papillomatosis (74% vs. 0%) [$p<0.001$], basal pigmentation (42% vs. 4%), and dysplsia and malinant canes (5% vs. 0%), respectively. were seen in, 97%, 95.7%, 74%, 42% and 5% of cases, respectively.

Conclusion In Bangladesh, long term arsenic exposure could increase the risk of certain kinds of cancers, some of them still unknown. It is therefore stressed that basic researches in histopathology of arsenic keratosis is patients particularly important in making the diagnosis.

Key words

Arsenicosis, histopathology

Introduction

The 'epidemic' occurrence of arsenicosis among people who have chronic exposure to arsenic through domestic consumption of contaminated ground water has been well reported in Bangladesh. The number of arsenicosis patients is increasing alarmingly day by day.¹⁻⁷ Ahmad *et al.*⁸ reported that about 6.6 % of the arsenicosis patients had neoplastic (cancerous and precancerous) skin lesions. Experts fear that, if the

exposure to arsenic continues, the morbidity and mortality due to arsenical carcinomas would rise.⁹

Elder¹⁰ indicated that the histopathological study could be taken to be a "gold standard" for most dermatological diagnoses and Kirkham¹¹ elucidated important histological features on arsenical keratosis and carcinoma. The present study was therefore undertaken to establish the relationship of histopathological findings with clinical arsenicosis, in Bangaldesh.

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Patients and methods

A total of 70 arsenicosis patients (arsenic-exposure group) and 20 healthy persons (control group) were included in this study. The patients selected had history of consumption of arsenic-contaminated water and showed typical features of cutaneous manifestations. Melanosis and keratosis are the two important skin lesions, which appear in almost all cases of arsenicosis. Since melanosis is not always associated with keratosis, but keratosis is always associated with melanosis, therefore biopsies were taken randomly from patients with keratosis. Skin biopsies were also obtained from 20 healthy individuals (controls) for comparison. Data obtained were statistically analyzed using χ^2 (Chi-square) test and Epi-info package system.

Results

Histopathological findings in 70 arsenicosis patients and 20 healthy controls are represented in **Table 1** and **Figure 1**. The dermatological manifestations are shown in **Figures 2-5** whereas **Figure 6** shows histopathological changes.

Discussion

The occurrence of cancer and precancerous skin lesions due to arsenic toxicity is well documented.¹² Malignant lesions due to chronic arsenic exposure through contaminated water have been reported from different parts of the world including Bangladesh.^{9,13,14,15} Histological examination of arsenical keratosis typically reveals hyperkeratosis with or without parakeratosis, acanthosis and enlargement of

Table 1 Histopathological findings of chronic arsenicosis

Findings	Patients (n= 70)	Controls (n= 20)	P value
Hyperkeratosis	70 (100%)	4 (20%)	<0.001
Parakeratosis	68 (97%)	2 (10%)	<0.001
Acanthosis	67(95.7%)	1 (5%)	<0.001
Papillomatosis	52 (74%)	0 (0%)	<0.001
Basal pigmentation	30 (42.8%)	4 (20%)	>0.05
Dysplasia & malignant changes	5 (7%)	0 (0%)	>0.1

rete ridges. In arsenical keratosis of the palms and soles, one may find, in some instances, only hyperkeratosis and acanthosis without evidence of nuclear atypicity. However, when one cuts deeper into the tissue block atypicity may become apparent.¹¹

Arsenical keratosis can be classified into two types:⁷ (1) a benign type with no cell atypia or with milder cellular atypia and (2) a malignant type consisting of lesions of Bowen's disease, basal cell carcinoma or squamous cell carcinoma. Skin histopathological findings of the present study agree with the study of Dhar *et al.*¹⁶ They showed that hyperkeratosis, parakeratosis, acanthosis, papillomatosis hypergranulosis and dysplastic changes were the most important and constant findings while basal pigmentation and dermal changes were inconstant findings. Similar result was also obtained from our study, which revealed that hyperkeratosis, parakeratosis and acanthosis were the most constant features in comparison to the control group ($p<0.001$). However, basal pigmentation replace dysplasia and malignant changes were inconstant findings

at $p > 0.05$ and > 0.1 level respectively. Ahmad *et al.*⁸ observed that in

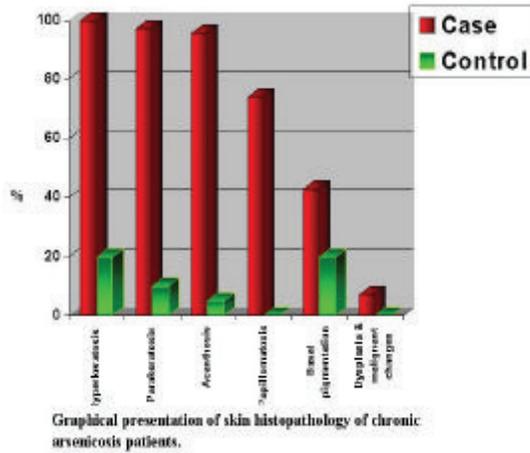


Figure 1 Comparison of different histological changes in the study group and control group.



Figure 2 Rain drop pigmentation over the trunk.

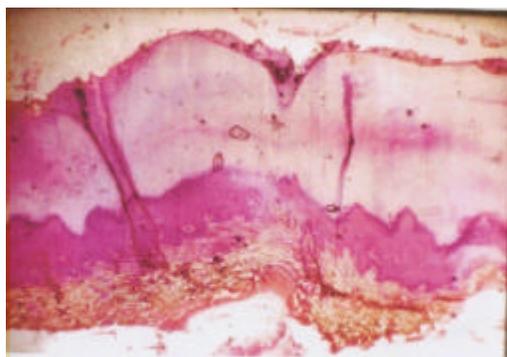


Figure 3 Palmo-plantar keratoderma.



Figure 4 Squamous cell carcinoma on the back of the heel.



Figure 5 Bowen's disease on the sole of the foot.**Figure 6** Histopathological changes in chronic arsenicosis.

Bangladesh about 6.6% of the arsenicosis patients had precancerous skin lesions and a very few (0.8%) had cancerous skin lesions. The investigators apprehended that if the arsenic exposure to drinking water continues the morbidity and mortality due to cancerous and precancerous lesions would be quite high. Rahman and Axelsen³ discussed arsenic kinetics in human health. They were of the opinion that the future magnitude of arsenic-caused skin cancer in Bangladesh is uncertain, but skin cancers have been reported in Taiwan, Chile, Mexico and elsewhere. The main cause of death due to chronic ingestion of arsenic in drinking water is internal cancers. Pulmonary cancer in vineyard workers exposed to an arsenic insecticide, and villagers exposed to arsenic-containing drinking water has been reported in earlier studies.^{18,19} In the latter series the onset of pulmonary cancer started 30 years after the arsenic exposure. That skin cancers are not fatal with appropriate treatment was the conclusion of the above researchers.

Experimental studies *in vitro* concerning the effects of inorganic arsenic on human epidermal cells have revealed that arsenic depresses premitotic DNA replication.

Moreover, arsenic seems to block predominantly DNA polymerase by attaching itself to sulfahydril groups. The damaging effect of arsenic on DNA has been thought to explain its carcinogenic effect.^{11,17}

Conclusion

More fundamental research in relation to the pathogenesis is particularly important in case of prolonged arsenic intake, since the available reports in Bangladesh demonstrate the existence of an arsenic-exposure-response relationship between magnitude of arsenic exposure and incidence of skin cancer and other manifestations, including keratosis and hyperpigmentation.

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